



## Research Letter

## Primary gallbladder carcinoma presenting as advanced-stage ovarian cancer

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Primary gallbladder carcinomas are rare and the prognosis is very poor. The incidence is 1–2% of all gastro-intestinal (GI) tract cancers [1]. Information on ovarian metastasis of primary gallbladder cancer is limited [2–13], partly because primary gallbladder cancers are rare, and partly because metastases from primary gallbladder cancer are mediated through either lymphatic or hematogenous routes. Since primary gallbladder cancers are mucinous tumors, there are problems with the differential diagnosis if mucinous ovarian carcinomas are found. Furthermore, primary or secondary ovarian mucinous tumors may present similar clinical symptoms, for example, non-specific GI symptoms or signs, and similar findings on imaging studies or tumor marker surveys. Before and during an operation, an accurate diagnosis sometimes cannot be made [14]. Herein, we present a case of secondary ovarian mucinous cancer emanating from primary gallbladder mucinous carcinoma.

An 84-year-old woman was sent to the emergency room because of diffuse abdominal pain and poor appetite. Clinical examination showed an acutely ill-looking woman with apparent peritoneal signs (diffuse tenderness and rebounding pain) associated with a lower abdominal mass. Ultrasound showed a 15-cm complex cystic mass in the right adnexa, but the uterus and the left ovary were normal. Computed tomography further identified this 15-cm ill-defined right adnexal heterogeneous mass with diffuse peritoneal seeding and

carcinomatosis. Serum tumor markers, including CA 125, CA 153, CA 199, and CEA were 327.3 U/mL, 29.0 U/mL, 218.0 U/mL, and 85.8 ng/mL, respectively. The other hematological and biochemical tests were normal. Upper and lower gastro-intestinal tract evaluations were negative.

Under the diagnosis of ovarian cancer, an exploratory laparotomy was done. A complex cystic right ovarian mass with a mucinous component was found, as well as diffuse carcinomatosis involving the entire lower and upper abdominal cavity, including the omentum, in which the inflamed gallbladder was embedded. Frozen section of the removed ovarian tumor favored the diagnosis of primary ovarian carcinoma, mucinous type. The patient underwent a suboptimal debulking surgery, including total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and retroperitoneal lymph node sampling, and multiple biopsies. The final pathology was primary gallbladder mucinous carcinoma.

Microscopic features showed hyperchromatic dysplasia of the mucinous glandular cells of the gallbladder; the mucinous tumor occupied the entire cavity of the gallbladder. The tumor had invaded whole layers of the gallbladder, and penetrated to the outside serosa and the attachment of the omentum. Other sections of the right ovary, appendix, omentum, abdominal wall, mesentery, and right pelvic lymph nodes all showed tumor metastases with floating mucinous tumor cells within an extensive mucin pool.

Using the American Joint Committee on Cancer (AJCC) staging for gallbladder cancer, the final diagnosis was gallbladder cancer stage IVB (pT4NxM1). However the patient died of disease 48 days after the operation.

This case report raised the following interesting issues. First, since 15% of ovarian cancers are secondary and 7–15%

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Table 1

A summary of published cases addressing primary gallbladder carcinoma with ovarian metastasis.

Author (case number)	Age at diagnosis (y)	Clinical presentations	Laterality	Tumor size	Pathologic finding
Meriden [2] (4)	56–69	Abd pain, Pel mass, LBO	Bil	—	—
Khunamornpong [3] (8)	47–83	Abd pain, vaginal bleeding, Pel mass	Bil	2.5–17 cm	Muc (6), End (1), Undiff (1)
Ayhan [4] (1)	33	Abd pain	Unil	3 cm	—
Jain [5] (1)	45	Abd mass	Bil	—	Muc
Jarvi [6] (1)	82	Abd pain	Bil	—	NOS
Carlomagno [7] (1)	38	Abd distention	Bil	—	Muc
Ricks [8] (1)	63	Pel mass, Abd pain, virilization	Bil	3–13 cm	—
Young [9] (5)	33–72	Abd pain, Pel mass	Bil	17, 19 cm	Muc (1)
Miyagui [10] (1)	43	Confusion	Bil	15 cm	Muc
Taranto [11] (1)	52	Pel mass	Bil	—	Muc
Petru [12] (2)			Bil	15	Muc (2)
Kumar [13] (2)	35, 62	Abd mass	Bil	17–20 cm	Muc (2)
Sun [current case] (1)	84	Abd pain, Pel mass	Bil	3, 15 cm	Muc

Abd = abdominal; Bil = bilateral; End = endometrioid; LBO = large bowel obstruction; Mun = mucinous; NOS = nonspecific; Pel = pelvic; Undiff = undifferentiated; Uni = unilateral.

of primary ovarian cancers are of a mucinous type, mucinous ovarian tumors present a challenge, and require a differential diagnosis between the primary and secondary types [15]. Second, intraperitoneal dissemination of primary gallbladder cancers is rare, and results in much rarer metastases to the ovary [2–13]. Third, patients with ovarian metastases from primary gallbladder cancers seldom have typical symptoms, for example, jaundice [3–5]. Fourth, tumor markers are not very useful in distinguishing one from the other, since CA-125, CA-199, and CEA levels might all be elevated in both conditions [3–8]. Fifth, radiological examinations, such as ultrasound, computed tomography, and magnetic resonance imaging, are also of little value [16], since many radiological features of primary gallbladder cancers with intraperitoneal carcinomatosis are easily masked by chronic cholecystitis or cholelithiasis. Therefore, these metastatic ovarian cancers from primary gallbladder cancers are often diagnosed initially as primary advanced-stage ovarian cancers [4–6]. Even with the assistance of pathologic evaluation, especially during frozen pathology, many cases are still considered to be primary ovarian cancers [3]. In Table 1 [2–14], we summarized the data of the currently available cases of primary gallbladder carcinoma mimicking advanced-stage ovarian cancers [2–13]. In fact, the rate of accurate preoperative diagnosis of these advanced primary gallbladder carcinomas accompanied with ovarian metastases was <30% [3].

When we deal with ovarian masses accompanied with carcinomatosis, the entire abdominal cavity, including the upper abdomen, should be evaluated carefully to explore all metastatic sites and lesions [17]. This procedure is important not only for the achievement of complete cytoreduction (optimal debulking surgery) for primary epithelial ovarian cancers [18], but also for identification of other non-ovarian primary sites (metastatic ovarian cancers) [14]. In this case, with the presence of a gallbladder mass that was embedded within the omentum and adjacent organs, and the difficulty of dissection between the gallbladder and the liver bed, the possibility of primary gallbladder carcinomas should be considered. However, only one grossly abnormal ovarian mass was found during the operation, and in addition, a complex

cystic mass with mucin extruding through the capsule of the right ovary might suggest the ovary as a primary site. These would not likely be diagnosed as metastatic ovarian cancers, which are usually bilateral, with surface implants, multinodular growth and more solid components [2–13]. The immunohistochemistry evaluation during the pathology review added little information. Common markers, including cytokeratin (CK) 7 or CK 20, were of little value.

The outcome of primary gallbladder cancer was significantly worse than that of primary ovarian cancer [1]. Unlike primary ovarian cancers [19], the role of surgical management in gallbladder cancer, including cholecystectomy, segmental liver resection, bile duct resection, and perihepatic lymphadenectomy, is limited for early-stage disease, and the use of either radiotherapy or chemotherapy provided little evidence of improvement in survival for patients with advanced primary gallbladder cancers [1].

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